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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,070	03/03/2006	Sutisak Kitareewan	DC0266US.NP	5026

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EXAMINER	
MARTIN, PAUL C	
ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
11/01/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/564,070	KITAREEWAN ET AL.	
	Examiner	Art Unit	
	PAUL C. MARTIN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim 8 is pending in this application and was examined on its merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/19/2010 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 remains rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshida *et al.* (1996) in view of Bard *et al.* (1977) for reasons of record set forth in the prior action.

Response to Arguments

Applicant's arguments filed 08/23/2010 have been fully considered but they are not persuasive.

The Applicant argues that the cited passage in Yoshida *et al.* teaches that "ATRA accelerates the degradation of PML-RARα in the proteasome pathway", in contrast to the instant invention which is directed to the identification of agents that induce the lysosome-dependent degradative pathway and that the instant assay requires the identification of agents that both destabilize lysosomes and increase PML-RARα (Remarks, Pg. 5, Lines 11-25 and Pg. 6, Lines 1-12).

This is not found to be persuasive for the following reasons, as discussed in the prior action, the claims are drawn to a method comprising (preamble/step ii) contacting a cell that expresses PML/RARα with an agent and detecting whether said agent increases PML/RARα degradation and contacting a cell that expresses PML/RARα with an agent and detecting whether said agent destabilizes lysosomes of the cell, as determined by vital staining of lysosomes or release of lysosomal proteins into the cytosol (preamble and step i).

Yoshida *et al.* teaches a method of identifying an agent that increases oncogenic protein degradation comprising contacting an APL (acute promyelocytic leukemia) cell that expresses PML/RARα with the anti-cancer agent ATRA (all-trans-retinoic acid) and detecting whether ATRA increases PML/RARα protein degradation. Yoshida et al. does not teach a method for identifying an agent which destabilizes lysosomes comprising contacting a cell that expresses PML/RARα with an agent and detecting whether the agent destabilizes lysosomes of the cell as determined by vital staining of lysosomes or release of lysosomal proteins into the cytosol.

Bard *et al.* teaches a method wherein cartilage cells are contacted with known anticancer retinoid compounds and detecting whether the retinoids destabilize lysosomes as determined by the release of lysosomal proteins into the cytosol and the resulting degradation of the cartilage matrix as a measure of toxicity. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of Yoshida et al. for identifying an anti-cancer agent that increases oncogenic protein degradation with the method of Bard *et al.* for identifying an anti-cancer agent which destabilizes lysosomes because it is prima facie obvious to combine two methods, each taught separately as useful for screening the same anti-cancer agent (retinoic acid) in order to form a single combined assay for detecting an anti-cancer agent which both destabilizes lysosomes and increases PML/RARα degradation. The MPEP states:

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be

used for the very same purpose ....

[T]he idea of combining them flows logically from their

having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846,850, 205 USPQ 1069, 1072 (CCPA 1980)

The Applicant argues that the whole of the teachings of Yoshida *et al.* show that PML/RARα is degraded by the proteosomal pathway, i.e., a non-lysosomal pathway. Therefore, Applicant asserts that the reference teaches away from doing what Applicant has done, determining whether an agent destabilizes lysosomes and increases lysosomal-dependent PML/RARα protein degradation and that there would be no motivation to look to the teachings of Bard *et al.* for determining whether an agent destabilizes lysosomes (Remarks, Pg. 6, Lines 19-27).

This is not found to be persuasive for the following reasons, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., determining whether an agent increases lysosomal-dependent PML/RARα protein degradation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Whatever pathway of degradation taught by Yoshida et al., the claims only require two steps. Yoshida *et al.* taught limitations found in the preamble and step ii, while Bard *et al.* was brought in for its teachings related to step i.

Both methods were drawn to screening for the same class of compounds, anti-cancer retinoids. Therefore, it is prima facie obvious to combine the two methods into a single screening method.

The Applicant argues that the Advisory action of 08/09/2010 asserts that one of ordinary skill in the art would recognize that if lysosomes were destabilized by ATRA, the degradation of aberrant proteins would have to proceed by another route, such as the non-lysosomal ubiquitin-proteosomal pathway, however Applicant asserts that the teachings of Bard *et al.* cannot be considered as pertinent to the teachings of Yoshida *et al.* as Bard *et al.* teaches that retinoids are toxic at higher than physiological concentrations while Yoshida et al. do not discuss the toxicity of ATRA in a method of differentiation of APL cells (Remarks, Pg. 6, Lines 28-31 and Pg. 7, Lines 1-14).

This is not found to be persuasive for the following reasons, in response to applicant's argument that the references are directed to different methods utilizing retinoid compounds at different concentrations, the fact remains that in combination the two references meet the limitations of claim 8 and *prima facie* reasoning exists as to why such a combination would be obvious as discussed in the prior actions and above.

Conclusion

No Claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

10/22/2010

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652